Association of MCM2 expression and RCB 0/I in hormonal receptor positive HER2 negative early breast cancer patients receiving neoadjuvant chemotherapy

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Background: Minimal residual cancer burden (RCB) after neoadjuvant chemotherapy is associated with better clinical outcomes in early breast cancer. Currently, no factor can reliably predict response to chemotherapy in hormonal receptor positive and HER2 negative breast cancer. Similar to Ki-67, high expression of mini-chromosome maintenance 2 (MCM2), a protein regulating initiation of DNA replication, is correlated with high proliferative index and worse clinical outcome in various cancer types, including breast cancer. This study aims to evaluate expression of MCM2 in pre-chemotherapy specimen for prediction of RCB 0/I in hormonal receptor positive and HER2 negative early breast cancer.

Methods: Electronic medical records of hormonal receptor positive and HER2 negative early breast cancer patients who received neoadjuvant chemotherapy followed by surgery between January 1, 2015 to December 31, 2020 in King Chulalongkorn Memorial Hospital were retrospectively reviewed. Immunostaining of MCM2 in pre-chemotherapy specimens and RCB index in post-chemotherapy specimens were evaluated for association. Image analysis for MCM2 expression was performed by Aperio Imagescope software. Univariate and multivariate analysis of clinicopathologic features and MCM2 were investigated for predicting response after neoadjuvant chemotherapy.

Results: Of 88 patients with early hormonal positive and HER2 negative breast cancer who received neoadjuvant chemotherapy, median age was 49 years (range 27-80) and 61.4% were premenopausal. Clinical stage cT4 and cN1 were 40% and 66.7%, respectively. 91.1% had invasive ductal carcinoma, 58.9% had histologic grade 2, 92.2% had >10% ER positivity and 22.2% had PR negative. 44% had 2 neoadjuvant chemotherapy regimens and anthracycline followed by paclitaxel was the most common regimen. RCB 0/I was observed in 7 patients (8.3%) and only 1 patient (1.2%) had RCB 0. In 72 available specimens for MCM2 and RCB evaluation, MCM2 expression >=40% was associated with RCB 0/I response in univariate analysis (OR = 18.33, 95% CI = 1.88-178.98, p-value = 0.012). Clinicopathologic features associated with MCM2 >40% were histologic grade 3, ER <=10%, negative PR status, and Ki-67 >=20%. No clinicopathologic factor was associated with RCB 0/I in multivariate analysis. Breast biomarkers in pre- and post-chemotherapy specimens were mostly constant. 3-year recurrence free survival was not significantly difference between patients with RCB 0/I and RCB II/III response.

Conclusions: MCM2 expression >=40% in pre-chemotherapy specimens was associated with higher RCB 0/I response in hormonal receptor positive and HER2 negative early breast cancer. Testing for MCM2 expression may predict neoadjuvant chemotherapy benefit in this breast cancer subtype. Further study with larger sample size is necessary to validate the result from this study.